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Dated 20 October 1999

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Request for grant of a patent

(See the notes on the back of this form. You can also get an explanatory leaflet from the Patent Office to help you fill in this form)

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The Patent Office

Cardiff Road
Newport
Gwent NP9 1RH

1. Your reference

Test ~~Directive~~ Strips for Small Volumes.

2. Patent application number

(The Patent Office will fill in this part)

9824627.53. Full name, address and postcode of the or of each applicant (*underline all surnames*)

CAMBRIDGE SENSORS LTD

DOWNHAMS HOUSE

DOWNHAMS LANE, CAMBRIDGE, CB4 1XT

Patents ADP number (*if you know it*)

If the applicant is a corporate body, give the country/state of its incorporation

UK 2668392.

4. Title of the invention

Test ~~Directive~~ Strips for Small Volumes5. Name of your agent (*if you have one*)

- NA -

"Address for service" in the United Kingdom to which all correspondence should be sent (*including the postcode*)

Cambridge Sensors Ltd

Downhams House

Downhams Lane, Cambridge, CB4 1XT, UK

Patents ADP number (*if you know it*)6. If you are declaring priority from one or more earlier patent applications, give the country and the date of filing of the or of each of these earlier applications and (*if you know it*) the or each application number

Country

Priority application number
(*if you know it*)Date of filing
(*day / month / year*)

- NA -

7. If this application is divided or otherwise derived from an earlier UK application, give the number and the filing date of the earlier application

Number of earlier application

Date of filing
(*day / month / year*)

- NA -

8. Is a statement of inventorship and of right to grant of a patent required in support of this request? (*Answer 'Yes' if:*

- a) *any applicant named in part 3 is not an inventor, or*
- b) *there is an inventor who is not named as an applicant, or*
- c) *any named applicant is a corporate body.*

See note (d))

YES.

9. Enter the number of sheets for _____ of the following items you are filing with this form.
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Continuation sheets of this form

Description 2

Claim(s) 0

Abstract 1

Drawing(s) 1

10. If you are also filing any of the following, state how many against each item.

Priority documents

Translations of priority documents

Statement of inventorship and right to grant of a patent (Patents Form 7/77)

NA

Request for preliminary examination and search (Patents Form 9/77)

Request for substantive examination
(Patents Form 10/77)

Any other documents
(please specify)

11.

I/We request the grant of a patent on the basis of this application.

Signature

J. McLarn

Date Nov 7th 1995.

12. Name and daytime telephone number of person to contact in the United Kingdom

J. McLarn

01223 - 424225

01223 - 420529 (fax).

Warning

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Notes

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- Write your answers in capital letters using black ink or you may type them.
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- If you have answered 'Yes' Patents Form 7/77 will need to be filed.
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Test Test Strips for Small Volumes

Diabetes is one of the most common endocrine conditions and leads to a requirement for sufferers to monitor their blood glucose level. This is chiefly achieved by use of small blood glucose test strips, which are known in the art. Some of these test strips use electrochemical reactions to carry out the analysis. Typically such reactions will consist of a redox enzyme, a mediator on a working electrode and a separate counter reference electrode.

There is a particular need for test strips that require very small amounts of blood since these are less painful for the patients. The invention described herein described is a test strip for blood glucose in which the sample requirement is very small and effective and efficient reaction kinetics are achieved by the application of the reagent layers in a novel manner.

In particular the enzyme and or co-factor may be applied in a mesh or membrane which is placed over the device such that when the sample is added the enzyme and co-factor are solubilised quickly and form an efficient reaction medium that can react with the separate electrodes of the test strip. In this manner the reaction will proceed rapidly and without diffusion barriers. This reaction configuration is particularly indicated in cases where the sample volume is low, the sample is viscous (such as with whole blood) and a rapid reaction is required.

In a typical embodiment of the invention the sensor test strip consist of two electrodes, one of which acts as a working electrode and another which acts as a counter reference electrode. The end of the working electrode that is exposed to the sample has a mediator in intimate contact with it. The reaction chamber consists of these two electrodes with a additional sheet overlaying the electrodes which has been pre-coated with the redox enzyme and any necessary co-factor for that enzyme. In addition the reaction chamber may be completed by the addition of further sheets of material and or the addition of surfactants or cell lysing materials (which may be placed in any one of the overlying aforesaid material sheets). In this manner the active enzyme is not coated onto the conductor which forms the working electrode but sits in the separate layer above it which, in turn, effectively forms the solution phase of the reaction chamber. A drawing of the configuration is enclosed Figure 1)

Other configurations are also possible to one skilled in the art including combinations of one or more of the cofactor, mediator or the enzyme coated onto the overlying mesh or membrane sheets depending upon the reaction kinetics of the various compounds.

In one example of the device a silver chloride, silver reference/counter electrode is located adjacent to a carbon electrode. A mediator for the enzyme cofactor NADH is then prepared and deposited onto the electrode electrode from aqueous solution by pipetting. A further layer containing NAD is then deposited onto the the working electrode.

A monofilament mesh material is then coated with a solution containing glucose dehydrogenase via pipetting, ink jet coating or dip coating and is then placed over the two electrodes to form a reaction chamber. This reaction chamber may be defined further by additional printing, by the use of a top layer to form an edge fill cavity.

In another embodiment of the device the mediator co-factor and the enzyme are all coated onto the working electrode directly and the sheet is such that is capable of filtering the whole

blood such that the active electrode sees a sample which is effectively free of whole blood cells; in this case the haematocrit dependency of the result is substantially reduced. Preferentially the cell filtering abilities of a selected membrane may be combined with the rapid kinetics of having the some or all of the active elements of the reaction (the enzyme, mediator and the co-factor)in the membrane to produce a highly effective device.

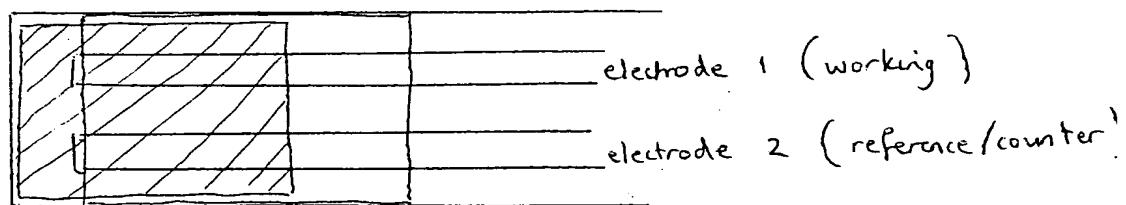
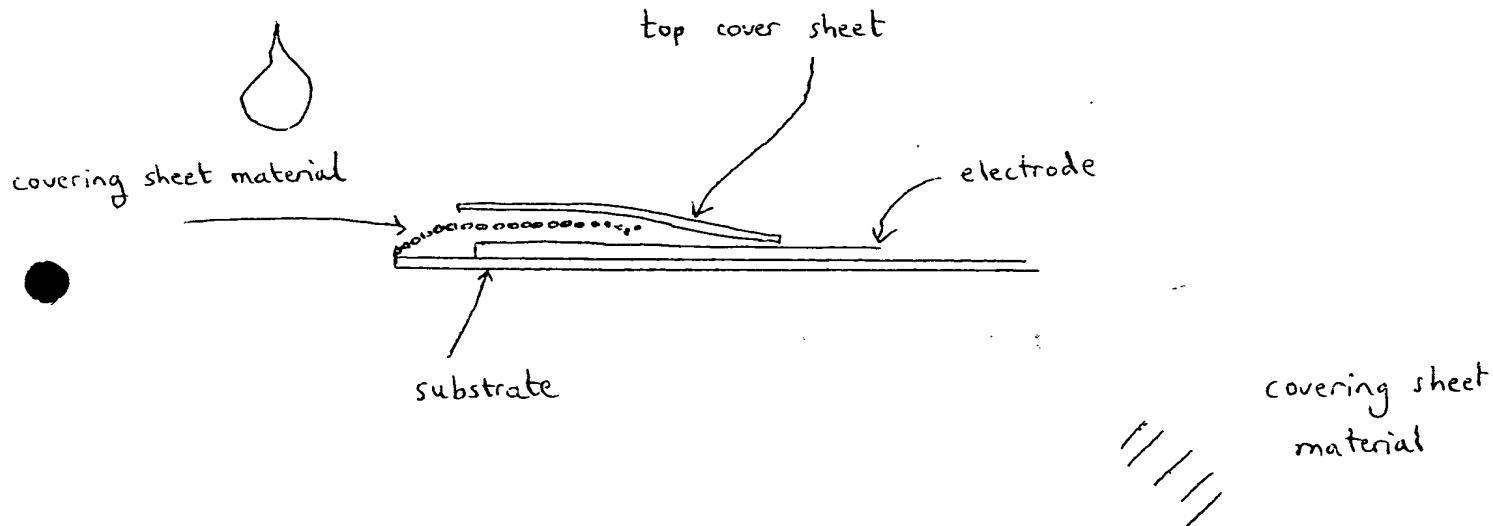
Abstract: Test Strips for Small Volumes

The invention provides a method for the realisation of test strips for substances that preferentially require very small samples to be used (down to under 1 micro-litre). This is achieved by the efficient reaction kinetics of test strips in which the reagents are rapidly solubilised and in particular having one of the active components of the reaction (enzyme or mediator) entrained in a permeable sheet layer that overlies the working electrode. In some configurations of the device this sheet layer defines a reaction chamber in which efficient reaction kinetics can occur. When combined with lateral turbulent flow, conditions are created which are approaching the conditions of efficient mixing in a stirred reaction chamber. This is particularly useful for small sample volumes, for dealing with viscous fluids such as blood, and for achieving rapid reactions.

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Figure 1

(whole blood)
sample applied to end

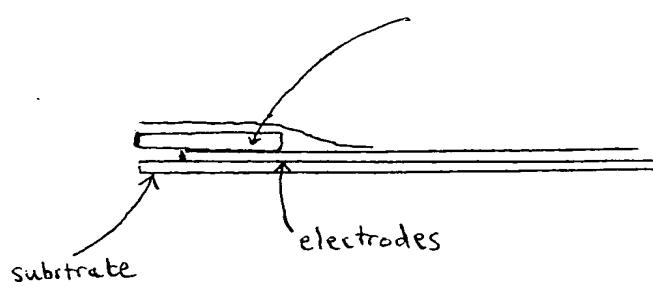


~~one of the~~

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Figure 1

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